REMARKS/ARGUMENTS

Claims 1-42 are pending in this application. Claims 1, 12, 28, 32, 33, 34, 39 and 42 have been amended without prejudice or acquiescence. Support for the amendment can be found in the Specification in paragraphs [0078]-[0080]. No new matter has been added. Claims 5, 16, 23-27 and 43-57 have been canceled without prejudice or acquiescence. Applicants retain the right to file a continuation application to any cancelled claims.

The issues outstanding in the application are as follows:

- Claims 23-27 were rejected under 35 U.S.C. § 112, first paragraph as allegedly not being enabled by the specification.

- Claims 24-27 and 32-38 were rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite.

- Claims 1, 7-8, 12, 20-21 and 42 were rejected under 35 U.S.C. § 102 as allegedly being anticipated by Kircheis.

- Claims 1-4, 7-15, 17-21, 28-31 and 41 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Johnston et al. (U.S. Patent No. 5,703,057) in view of Kircheis et al.

- Claims 32-41 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Johnston et al. (U.S. Patent No. 5,703,057) in view of Kircheis et al. and Wiener et al. (U.S. Patent No. 6,348,449).

Applicants respectfully traverse the outstanding rejections, and Applicants respectfully request reconsideration and withdrawal thereof in light of the amendments and remarks contained herein.

SUMMARY OF TELEPHONIC INTERVIEW

At this time, Applicants wish to thank the Examiner for his time on Tuesday, June 3, 2003 in which the Agent for the Applicants, Melissa Acosta and the Examiner discussed via telephone the rejections of the office action.

Regarding the 112, first paragraph rejections, Applicants discussed with the Examiner canceling claims 23-27. Thus, this rejection is moot.

The Applicants also discussed the prior art rejections, specifically Kircheis et al. Applicants discussed the difference between Kircheis et al. and the present invention is that the present invention is drawn to a composition that comprises DNA bound to an aggregated protein-polycationic polymer conjugate that forms a DNA particle or a particulate composition. It was also discussed that particulate compositions are known to be insoluble. Kircheis et al. is drawn to soluble compositions. Applicants and the Examiner discussed adding the term "DNA particulate" to further distinguish the present invention over Kircheis.

I. Rejection under 35 U.S.C. § 112, first paragraph

The Examiner has rejected claims 23-27 under 35 U.S.C. § 112 first paragraph as allegedly not being enabled by the specification. Applicants respectfully traverse.

In order to advance prosecution of this application, Applicants have canceled claims 23-27 without prejudice or acquiescence. In light of the amendments, the rejection is moot and Applicants respectfully request withdrawal of the 35 U.S.C. § 112 rejection.

II. Rejection under 35 U.S.C. § 112, second paragraph

The Examiner has rejected claims 24-27 and 32-38 under 35 U.S.C. § 112 second paragraph as allegedly being indefinite. Applicants respectfully traverse.

In order to advance prosecution of this application, Applicants have canceled claims 24-27 without prejudice or acquiescence. In light of the amendments, the rejection is moot and Applicants respectfully request withdrawal of the 35 U.S.C. § 112 rejection.

In claim 32, the Examiner has stated that the phrase "the second vector comprises a cytokine expression vector" is unclear. In order to advance prosecution of this application, Applicants have amended claims 32-34 without prejudice or acquiescence. No new matter has been added. In light of the amendments, Applicants respectfully request withdrawal of the 35 U.S.C. § 112 rejection.

III. Rejection under 35 U.S.C. § 102

The Examiner has rejected claims 1, 7-8, and 42 under 35 U.S.C. § 102 as being allegedly anticipated by Kircheis *et al.* The Examiner states that Kircheis et al. disclose the preparation of DNA complexes of ligand-polyethylenimine conjugates for transfection of cultured cells. Applicants respectfully traverse.

Anticipation of a claim is only established where "each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

Kircheis et al. teach the use of a soluble delivery system to deliver DNA to cells via receptor-mediated endocytosis. It is well known by those of skill in the art that polycations are water-soluble complexes and that conjugation of DNA to a polycation neutralizes the negative charge of the DNA to condense the DNA and increase solubility. Still further, it is known that conjugation of a specific ligand, such as transferrin, to the DNA complex will increase the efficiency because the ligand is targeted to a specific cell surface receptor, such as the transferrin receptor. In fact on page 416, first column, Kircheis et al. states that transfection complexes should be highly soluble. The soluble DNA complex of Kircheis et al. is the opposite of the present invention.

The present invention teaches a DNA particle or particulate that is formed by binding to the aggregated protein-polycationic polymer. The aggregated protein aids in the particulate formation. (See paragraph [0078]-[0080]). Thus, the DNA particle or particulate of the present invention is insoluble, which is the opposite of the soluble particle taught by Kircheis et al.

As discussed with the Examiner during the telephonic interview, the claims in the present application are directed to particulate compositions. One skill in the art realizes that a composition that comprises DNA bound to an aggregated protein-polycationic polymer conjugate forms a DNA particle or a particulate composition. Particulate compositions are known to be insoluble. The definition of the term "particulate" is solid matter particles or formed bodies as contrasted with the surrounding liquid or semiliquid material (See page 1329 of Stedman's Medical Dictionary 27th Edition, 2000). Thus, the DNA particle of the present invention is not similar to the soluble composition that is formed by Kircheis et al.

In order to further the prosecution of the present application, Applicants have amended claims 1 and 42 without acquiescence and prejudice to indicate that the expression vector bound to an aggregated protein-polycationic polymer conjugate forms a DNA particulate. Therefore, since the limitation of a DNA particulate is absent in Kircheis *et al.*, Kircheis *et al.* is precluded from anticipating the present claims. Thus, the rejection of claims is improper, and withdrawal of the rejection is respectfully requested.

IV. Rejection under 35 U.S.C. § 103(a)

The Examiner has rejected claims 1-4, 7-15, 17-21, and 28-31 under 35 U.S.C. § 103 as being allegedly being obvious over Johnston *et al.* (U.S. Patent No. 5,703,057) in view of Kircheis *et al.* Applicants respectfully traverse.

To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). Johnston teaches expression vectors encoding antigens prepared from pathogenic viruses, and the expression of such antigens in mammalian cells. Applicants teach expression vectors, including vectors which express antigens derived from pathogenic viruses for expression in mammalian cells. The Johnston reference does not teach such vectors bound to an aggregated protein polycationic polymer conjugate.

The Kircheis *et al.* reference teaches protein conjugated to polycationic polymers bound to DNA. The Kircheis *et al.* reference does not teach protein aggregates that are used to form DNA particulates. In fact, Kircheis et al. teach away from the present invention. Kircheis et al. teach that transfection complexes must be highly soluble, which is the opposite of the present invention. Thus, the combination of Kircheis *et al.* and Johnston does not produce the Applicants' invention, as a DNA particulate is not taught or suggested.

In light of the above arguments, Applicants respectfully request withdrawal of the 35 U.S.C. § 103 rejection.

V. VI. Rejection under 35 U.S.C. § 103(a)

Claims 32-41 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Johnston *et al.* (U.S. Patent No. 5,703,057) in view of Kircheis *et al.* and Wiener *et al.* (U.S. Patent No. 6,348,449). Applicants respectfully traverse.

To establish prima facie obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). Johnston teaches expression vectors encoding antigens prepared from pathogenic viruses, and the expression of such antigens in mammalian cells. Applicants teach expression vectors, including vectors which express antigens derived from pathogenic viruses for expression in mammalian cells. The Johnston reference does not teach such

vectors bound to an aggregated protein polycationic polymer conjugate. The Kircheis *et al.* reference does not teach protein aggregates that are used to form DNA particulates, for the reasons outlined above. The Weiner reference teaches genetic constructs that encode a target protein and further include genes which enhance the immune response, such as cytokines. The Weiner reference does not teach protein aggregates that are used to form DNA particulates. The combination of Johnston, Kircheis *et al.*, and Weiner does not yield the Applicants' invention, as the DNA particulate is not taught. Additionally, there is no suggestion in any of these references that a DNA particulate is desirable as a DNA delivery method. Thus, absent the teaching or suggestion of all the limitations of the Applicants' invention, the Examiner has failed to establish a *prima facie* case of obviousness.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue.

Applicant believes no fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 06-2375, under Order No. 10004014 from which the undersigned is authorized to draw.

Dated: July 9, 2003

Respectfully submitted,

By

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rus of the cerebral...

...the other two being the orbital part and opercular part. SYN ...triangularis [TA].
...tympanic p. of temporal bone, SYN tympanic *plate* of temporal bone.
umbilical p. of left branch of portal vein [TA], the highly branched part of the left branch of the portal vein; the round and venous ligaments attach to this part. SYN pars umbilicalis rami sinistri venae portae hepatis [TA].
uterine p. of uterine tube [TA], the part of the uterine tube located within the wall of the uterus. SYN pars uterina tubae uterinae [TA].
uveal p. of trabecular reticulum, SYN uveal p. of trabecular tissue of sclera.
uveal p. of trabecular tissue of sclera [TA], the posterior part of the trabecular reticulum, located between the scleral spur, the ciliary body, and the anterior surface of the iris. SYN pars uvealis reticuli trabecularis sclerae [TA], uveal p. of trabecular reticulum.
vagal p. of accessory nerve, *official alternate term for cranial root of accessory nerve: SEE accessory *nerve* [CN XI].
vaginal p. of cervix [TA], the part of the cervix uteri contained within the vagina. SYN portio vaginalis cervicis [TA].
ventral p. of intertransversarii laterales lumborum (muscles) [TA], portions of the lateral intertransversarii of the lumbar region connecting the costal elements of the transverse processes of the lumbar vertebrae. SYN pars ventralis musculi intertransversarii lateralium lumborum [TA].
ventral p. of pons, SYN basilar p. of pons.
vertebral p. of the costal surface of the lungs [TA], the p. of the medial surface of the lung in contact with the vertebral bodies. SYN pars vertebralis faciei costalis pulmonis [TA].
vertebral p. of diaphragm, SYN lumbar p. of diaphragm.
vestibular p. of vestibulocochlear nerve, SYN vestibular *nerve*.

part. aeq. Abbreviation for L. *partes aequales*, in equal parts (amounts).

par·tes (par′tēz). Plural of pars.

par·the·no·gen·e·sis (par′the-nō-jen′ĕ-sis). A form of nonsexual reproduction, or agamogenesis, in which the female reproduces its kind without fecundation by the male. SYN apogamia, apogamy, apomixia, virgin generation. [G. *parthenos*, virgin, + *genesis*, product]

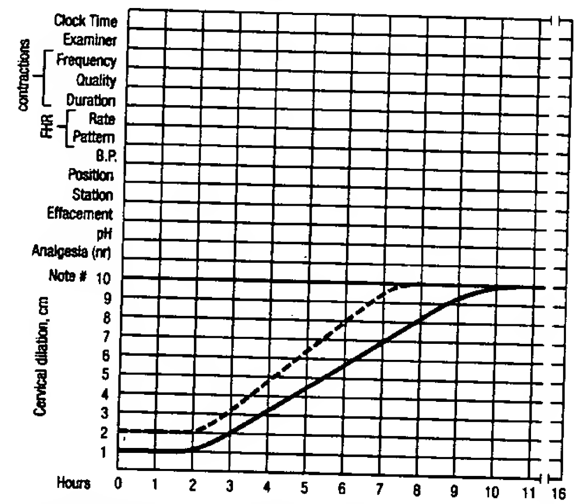
par·the·no·pho·bia (par′the-nō-fō′bē-ă). Morbid fear of girls. [G. *parthenos*, virgin, + *phobos*, fear]

par·ti·cle (par′ti-kl). **1.** A very small piece or portion of anything. **2.** An elementary p. such as a proton or electron. [L. *particula*, dim. of *pars*, part]
alpha p. (α), a p. consisting of two neutrons and two protons, with a positive charge (2e⁺); emitted energetically from the nuclei of unstable isotopes of high atomic number (elements of mass number from 82 up); identical to the helium nucleus. SYN alpha ray.
beta p., an electron, either positively (positron, β^+) or negatively (negatron, β^-) charged, emitted during beta decay of a radionuclide. SEE ALSO cathode *rays*, under *ray*. SYN beta ray.
chromatin p.'s, fine bluish dots thought to represent remnants of the nucleus, occasionally seen in stained erythrocytes.
core p., p. released by partial enzymatic digestion of chromatin.
Dane p.'s, the larger spherical forms of hepatitis-associated antigens; they compose the virion of hepatitis B virus, containing a 27-nm "core" in which DNA-dependent DNA polymerase and circular, double-stranded DNA have been found.
defective interfering p., an incomplete virus that is unable to replicate and interferes with replication of an infectious virus.
D.I. p., abbreviation for defective interfering p.
electron transport p.'s (ETP), fragments of mitochondria still capable of transporting electrons. SYN submitochondrial p.'s.
elementary p., (1) SYN platelet; (2) one of the units occurring on the matrical surface of mitochondrial cristae; the head of the p., which measures about 9 nm, attaches to the membrane of the crista by a stalk 5 nm long; the p.'s may be concerned with the electron transport system.
kappa p.'s, inheritable cytoplasmic symbionts, once thought to be p.'s mainly or exclusively of DNA, occurring in some strains of *Paramecium;* capable of producing a product lethal to other strains.
signal recognition p. (SRP), a small RNA-protein complex that interacts with the signal sequence of nascent secretory proteins. Binding of the signal recognition p. results in arrest of translation until interaction with docking protein, an integral part of the endoplasmic reticulum membrane.
submitochondrial p.'s, SYN electron transport p.'s.
Zimmermann elementary p., obsolete term for platelet.

par·tic·u·late (par-tik′ū-lāt). Relating to or occurring in the form of fine particles.

par·tic·u·lates (par-tik′ū-lats). Formed elements, discrete bodies, as contrasted with the surrounding liquid or semiliquid material; e.g., granules or mitochondria in cells.

par·to·gram (par′tō-gram). Graph of labor parameters of time and dilation with alert and action lines to prompt intervention if the curve deviates from expected. SYN Friedman curve, labor curve. [L. *partus*, childbirth, + -gram]



partogram: flowsheet for charting labor progress, FHR = fetal heart rate

par·tu·ri·ent (par-too′rē-ent). Relating to or in the process of childbirth. [L. *parturio*, to be in labor]

par·tu·ri·fa·cient (par-toor-ē-fā′shent). **1.** Inducing or accelerating labor. **2.** An agent that induces or accelerates labor. SYN oxytocic (2). [L. *parturio*, to be in labor, + *facio*, to make]

par·tu·ri·tion (par-toor-ish′ŭn). SYN childbirth. [L. *parturitio*, fr. *parturio*, to be in labor]

part. vic. Abbreviation for L. *partes vicibus*, in divided doses.

pa·ru·lis, pl. **pa·ru·li·des** (pă-roo′lis, -li-dēz). SYN gingival *abscess*. [G. *paroulis*, gumboil, fr. *para*, beside, + *oulon*, gum]

par·um·bil·i·cal (par′ŭm-bil′i-kăl). SYN paraumbilical.

par·u·re·sis (par-ū-rē′sis). Inhibited urination, especially in the presence of strangers. [para- + G. *ourēsis*, urination]

par·val·bu·min (par-val-bū′min). Any of a group of small water-soluble calcium-binding proteins distinct from calmodulin and other calcium-binding proteins; found in the brain, skeletal muscle, and retina, but not in the heart, liver, or spleen, of various species. [L. *parvus*, small, + albumin]

Par·vo·bac·te·ri·a·ce·ae (par′vō-bak-tēr-ē-ā′sē-ē). A family name regarded as a former name for the bacterial family Brucellaceae. No type genus has ever been proposed for the family P.

par·vo·cel·lu·lar (par-vō-sel′ū-lăr). Relating to or composed of cells of small size. [L. *parvus*, small, + Mod. L. *cellularis*, cellular]

par·vo·line (par′vō-lēn). A ptomaine, $C_9H_{13}N$, from decaying fish.

Par·vo·vir·i·dae (par-vō-vir′i-dē). A family of small viruses con-